REMARKS

Claim 1 has been amended to recite "[a] method of optimizing performance of a fermentation process involving a complex nutrient mixture comprising:

(a) calculating a feed concentration of the complex nutrients;

(b) periodically stopping a supply of each nutrient in a complex nutrient mixture to a culture of microorganisms until a metabolic activity of the microorganisms decreases by a preset percentage;

and

(c) adjusting the amount of each nutrient supplied to the microorganisms with an optimization routine, wherein a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients is calculated and the feed concentration of the complex nutrients and the total quantity of the complex nutrients are treated as separate control variables that are calculated and adjusted simultaneously." Support for these amendments is found in original claims 1 and 6 and in the specification at, for example, page 1, para. [0002], page 4, para. [0011], page 8, para. [0019], page 21, para. [0069] to page 22, para. [0071], and Example 1. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01 (o) and (l).

Claim 4 has been amended to recite "[a] method according to claim 1, wherein the optimization routine comprises:

(a) generating a flow chart with a co-ordination controller for generating control variables using a negative-pulse response technique;

(b) generating response times; and

(c) using the response times to form an input variable Q_{sens}, which is obtained by dividing an actual pulse response time Δt_i by a pulse response time Δt_{i-1} in a previous

cycle, measured with another complex nutrient." Support for these amendments is found in original claim 4 and in the specification at, for example, page 10, para. [0025]. (*Id.*).

PRIORITY:

We thank the Examiner for his acknowledgment "of applicant's claim for foreign priority based on European Patent Office (EPO) Application No. 00123710.6." (Paper No. 20061022 at 2). The Examiner stated, however, "the priority document was apparently lost [by the PTO] ...," and the Examiner requested that Applicants file another a copy. (*Id.*). In accordance with the Examiner's request, another copy of EPO Application No. 00123710.6 is being currently filed herewith as Exhibit 1.

For the reasons set forth above, it is submitted that Applicants have complied with all rules regarding priority under 35 U.S.C. § 119, and it is requested that the Examiner confirm on the record that the claim to benefit has been perfected.

§112, SECOND PARAGRAPH REJECTION:

Claims 1, 3, 4, and 7-8 have been rejected under 35 U.S.C. §112, second paragraph. (Paper No. 20061022 at 3).

In making the rejection, the Examiner asserted that "it is unclear as to the intended meaning of 'a ratio ... is treated ... but adjusted' such that one skilled in the art would know in what way said ratio 'is treated as a separate control variable but is adjusted simultaneously.'" (*Id.*).

With a view towards furthering prosecution, step (c) of claim 1 has been amended to recite "adjusting the amount of each nutrient supplied to the microorganism with an optimization routine, wherein a ratio between the feed concentration of the

complex nutrients and the total quantity of the complex nutrients is calculated and the feed concentration of the complex nutrients and the total quantity of the complex nutrients are treated as separate control variables that are calculated and adjusted simultaneously." In view of the foregoing amendments, the rejection of claim 1 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner also asserted, with respect to claim 1, that the limitation "a separate control variable" lacks a proper "antecedent basis." (*Id.*).

In view of the foregoing amendments, the rejection of claim 1 is rendered moot. However, applicants' note that the indefinite article "a" or "an" can be used to introduce a new limitation in a claim. *See* MPEP § 2173.05(e). If applicants' had been referring to a previously recited limitation they would have used the definite article "the" or "said."

The Examiner asserted, with respect to claim 4, that the limitation "generating control variables" lacks a proper "antecedent basis." (Paper No. 20061022 at 3).

It is respectfully submitted that the Examiner is mistaken. There is no lack of antecedent basis in claim 4. The phrase "generating control variables" is being introduced into the claim ***for the first time***. Therefore, because the phrase is being introduced for the first time in the claim, there is no antecedent basis problem. *See* MPEP § 2173.05(e).

The Examiner also asserted, with respect to claim 4, that the limitation "an actual pulse response time Δt_i" lacks a proper "antecedent basis." (Paper No. 20061022 at 3).

It is respectfully submitted that the Examiner is mistaken. There is no lack of antecedent basis in claim 4. The phrase "an actual pulse response time Δt_i" is being introduced into the claim ***for the first time***. Therefore, because the phrase is being introduced for the first time in the claim, there is no antecedent basis problem. *See* MPEP § 2173.05(e). It is respectfully submitted that it is irrelevant that "claim 4 previously recites 'response times.'" (Paper No. 20061022 at 3).

The Examiner also asserted, with respect to claim 4, that the limitation "a pulse response time Δt_{i-1}" lacks a proper "antecedent basis." (*Id.* at 4).

It is respectfully submitted that the Examiner is mistaken. There is no lack of antecedent basis in claim 4. The phrase "a pulse response time Δt_{i-1}" is being introduced into the claim ***for the first time***. Therefore, because the phrase is being introduced for the first time in the claim, there is no antecedent basis problem. *See* MPEP § 2173.05(e). It is respectfully submitted that it is irrelevant that "claim 4 previously recites 'response times.'" (Paper No. 20061022 at 4).

The Examiner also rejected claim 4 under 35 U.S.C. § 112, second paragraph, for the recitation of "a respective other complex nutrient." (*Id.*). In particular, the Examiner asserted that the meaning of "a respective other" was unclear. (*Id.*). With a view towards furthering prosecution, claim 4 has been amended to delete the rejected language. In view of the foregoing, the rejection has been rendered moot and should be withdrawn.

The Examiner also rejected claims 1, 3, 4, 7, and 8 "as being incomplete for omitting essential steps." (Paper No. 20061022 at 4). The Examiner asserted that "[t]he omitted essential steps appear to be: (i) calculation of control variable(s), and (ii)

calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, since the instant claims do not indicate which calculations of the preceding steps would indicate a ratio between the feed concentration and the total quantity." (*Id.*).

With a view towards furthering prosecution, step (c) of claim 1 has been amended to explicitly recite "adjusting the amount of each nutrient supplied to the microorganism with an optimization routine, wherein a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients ***is calculated*** and the feed concentration of the complex nutrients and the total quantity of the complex nutrients are treated as separate control variables that ***are calculated and adjusted simultaneously***." In view of the foregoing amendments, the rejection of claim 1 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

REJECTIONS UNDER 35 USC § 102:

Claims 1, 3, 4, and 7-8 were rejected under 35 USC § 102(b) as anticipated by Fleury *et al.*, "Modeling And Control Strategies For The Transformation Of D-Sorbitol To L-Sorbose On A Laboratory Bioreactor," Advances in Bioprocess Engineering, Netherlands: Kluver Academic Publishers, pp. 313-320 (1994) ("Fleury"). (Paper No. 20061022 at 5).

For the reasons set forth below, the rejection, has been rendered moot.

Fleury discloses "the formulation and adjustment of a mathematical model and the design of a control strategy for a fermentation process, the bioxidation of D-sorbitol to L-sorbose ...." (Page 313, para. 1). The "procedure to convert glucose into L-ascorbic acid is a combination of several stages of chemical reactions, physico-

chemical operations and a single biochemical step - the microbial oxidation of D-sorbitol to L-sorbose - performed by a bacterial strain of *Gluconobacter oxydans*." (*Id.*). "The culture media used ... was prepared with sorbitol, yeast extract and salts." (Page 314, para. 1).

In making the rejection, the Examiner asserted that "[c]laim 1, step (c), now recites 'adjusting the amount ... with an optimization routine, wherein a ratio ... is treated as a separate control variable but is adjusted simultaneously.' It is noted that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, *therefore the Examiner has interpreted this limitation broadly*." (Paper No. 20061022 at 5) (emphasis added).

The Examiner asserted that Fleury discloses:

> [F]eed concentrations for biomass (X), sorbose (p), sorbitol (S_1), and yeast (S_2), etc. (i.e. complex nutrients) obtained over time [Fig. 1]. Webster's dictionary (10^{th} edition) defines "ratio", *inter alia,* as the relationship in quantity, size, or amount between two or more things, therefore each of the above concentrations taught by Fluery et al. is clearly a teaching for a "ratio" between the respective complex nutrient and the total biomass of the complex nutrients, as in claim 1. Fluery et al. also teach concentrations used as separate model parameters (i.e. control variables) [Table 3]. Fluery et al. also teach an optimization equation comprising an input ratio of quantitative measurements for sorbose and sorbitol (i.e. Q_{sens}) [p.317, EQN (22)] and related pulse response times [Fig. 4], as in claim 1. Fluery et al. also teach a ratio between lowest and highest eigenvalues for D-sorbitol conversion to L-sorbose for system optimization and partitioning [p.317, Col. 2, ¶2], which also equates to a ratio treated as a separate control variable as in claim 1. Furthermore, Fluery et al. teach sorbose (p) and sorbitol (S1) measurements containing delays that are included into the simulation after an actualization cycle [p.318, Simulations and Results, Section 1], which is a teaching for fit delays and previous cycles as in amended claim 4. (Paper No. 20061022 at 5-6).

As is well settled, anticipation requires "identity of invention." *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply,* 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.,* 221 USPQ 481, 485 (Fed. Cir 1984). "Moreover, it is incumbent upon the Examiner to ***identify where each and every facet*** of the claimed invention is disclosed in the applied reference." *Ex parte Levy*, 17 USPQ2d 1461, 1462 (BPAI 1990). The Examiner is required to point to the disclosure in the reference "***by page and line***" upon which the claim allegedly reads. *Chiong v. Roland*, 17 USPQ2d 1541, 1543 (BPAI 1990).

With a view towards furthering prosecution, we note that the subject matter of previously *non-rejected*, now cancelled, claim 6 has been incorporated into claim 1, from which claims 3, 4, 7, and 8 either directly or indirectly depend.

In particular, claim 1 now recites "[a] method of optimizing performance of a fermentation process involving a complex nutrient mixture comprising:

(a) calculating a feed concentration of the complex nutrients;

(b) periodically stopping a supply of each nutrient in a complex nutrient mixture to a culture of microorganisms until a metabolic activity of the microorganisms decreases by a preset percentage;

and

(c) adjusting the amount of each nutrient supplied to the microorganisms with an optimization routine, *wherein a ratio between the feed concentration of the complex*

nutrients and the total quantity of the complex nutrients is calculated and the feed concentration of the complex nutrients and the total quantity of the complex nutrients are treated as separate control variables that are calculated and adjusted simultaneously." With these amendments, the Examiner's concern regarding claim 1, *i.e.*, "that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients," is rendered moot.

Furthermore, it is respectfully submitted that Fleury ***fails*** to disclose or suggest that "*a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***is calculated*** *and the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***are treated as separate control variables that are calculated and adjusted simultaneously***" as recited in amended claim 1.

In sum, Fleury does not disclose each and every element of amended claims 1, 3, 4, 7, and 8. Accordingly, it is respectfully submitted that the rejection of claims 1, 3, 4, 7, and 8 has been rendered moot and should be withdrawn.

Claims 1 and 3 were rejected under 35 USC § 102(a) as anticipated by Miskiewicz *et al.*, "A Fuzzy Logic Controller To Control Nutrient Dosage In A Fed-Batch Baker's Yeast Process," Biotechnology Letters, vol. 22, pp. 1685-1691 (2000) ("Miskiewicz"). (Paper No. 20061022 at 6).

For the reasons set forth below, the rejection, has been rendered moot.

Miskiewicz discloses "[a] fuzzy logic controller designed to control glucose feeding in a fed-batch baker's yeast process .... Feeding is carried out in portions and the controller determines the time at which glucose should be added and computes the

size of the portion to provide the maximum glucose uptake rate. Moreover, the controller detects and prevents the occurrence of overdosage." (Abstract). The "fuzzy logic controller ... supervise[s] the inflow of glucose feed so as to provide a very high yield and a high specific growth rate of baker's yeast cultured in a laboratory-scale fermenter." (Page 1685, line 24 to page 1686, line 3).

In making the rejection, the Examiner asserted that "[c]laim 1, step (c), now recites 'adjusting the amount ... with an optimization routine, wherein a ratio ... is treated as a separate control variable but is adjusted simultaneously.' It is noted that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, *therefore the Examiner has interpreted this limitation broadly*." (Paper No. 20061022 at 6) (emphasis added).

> The Examiner asserted that Miskiewicz discloses:
>
> > [C]alculation of consecutive nutrient dosage based on multiple inputs [p.1686, col. 2, lines 24-26] and an optimization routine using a fuzzy logic controller with nutrient feed input variables to optimize yield (i.e. output) [p. 1685, col. 2, paragraph 2; and p.1686, col. 1, paragraph 1], and define relationships between input concentrations and the yield control variables [Fig. 4, 5, and 6]. Webster's dictionary (10^{th} edition) defines "ratio", *inter alia,* as the relationship in quantity, size, or amount between two or more things. Therefore, the above "relationship" taught by Miskiewicz et al. is a teaching for a "ratio" between the respective complex nutrient and the yield (i.e. quantity) of the complex nutrients, as in claim 1. (Paper No. 20061022 at 6-7).

As stated above, anticipation requires "identity of invention." *Glaverbel Societe Anonyme,* 33 USPQ2d at 1498. Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim. *Marshall,* 198 USPQ at 346; *Lindemann Maschinenfabrik GMBH,* 221 USPQ at 485. "Moreover,

it is incumbent upon the Examiner to ***identify where each and every facet*** of the claimed invention is disclosed in the applied reference." *Levy*, 17 USPQ2d at 1462. The Examiner is required to point to the disclosure in the reference "***by page and line***" upon which the claim allegedly reads. *Chiong*, 17 USPQ2d at 1543.

With a view towards furthering prosecution, we note again that the subject matter of previously *non-rejected*, now cancelled, claim 6 has been incorporated into claim 1, from which claim 3 directly depends.

In particular, claim 1 now recites "[a] method of optimizing performance of a fermentation process involving a complex nutrient mixture comprising:

(a) calculating a feed concentration of the complex nutrients;

(b) periodically stopping a supply of each nutrient in a complex nutrient mixture to a culture of microorganisms until a metabolic activity of the microorganisms decreases by a preset percentage;

and

(c) adjusting the amount of each nutrient supplied to the microorganisms with an optimization routine, *wherein a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients is calculated and the feed concentration of the complex nutrients and the total quantity of the complex nutrients are treated as separate control variables that are calculated and adjusted simultaneously*." With these amendments, the Examiner's concern regarding claim 1, *i.e.*, "that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients," is rendered moot.

Furthermore, it is respectfully submitted that Miskiewicz ***fails*** to disclose

or suggest that "*a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***is calculated*** *and the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***are treated as separate control variables that are calculated and adjusted simultaneously***" as recited in amended claim 1.

In sum, Miskiewicz does not disclose each and every element of claims 1 and 3. Accordingly, it is respectfully submitted that the rejection of claims 1 and 3 has been rendered moot and should be withdrawn.

REJECTION UNDER 35 USC § 103:

Claims 1, 3, 4, and 7-8 were rejected under 35 USC § 103 as being unpatentable over Kurokawa *et al.*, "Growth Characteristics In Fed-Batch Culture Of Hybridoma Cells With Control Of Glucose And Glutamine Concentrations," Biotechnology And Bioengineering, vol. 44, pages 95-103 (1994) ("Kurokawa") in view of Fleury and Johnson *et al.*, U.S. Patent No. 6,792,336 ("Johnson"). (Paper No. 20061022 at 7-9).

The rejection respectfully is traversed.

Kurokawa discloses "[a]n online system using HPLC [ ] developed for the measurement of glucose, glutamine, and lactate in a culture broth. Using the system, the glucose and glutamine concentrations were controlled simultaneously by an adaptive-control algorithm within the ranges of 0.2 to 2.0 and 0.1 to 0.6 g/L, respectively. When the glucose concentration was controlled at the low level of 0.2 g/L, the intracellular lactate dehydrogenase activity decreased by one-half and the lactate concentration by one-third, whereas the uptake rates of serine and glycine were about

twice as high, compared with the amounts when the glucose concentration was controlled at 1.0 g/L." (Abstract). Figure 3 shows the results of the "[g]lucose concentration [ ] controlled at 0.2 g/l ... using the adaptive control strategy." (Page 98, lines 37-38). "Table II shows a comparison of LDH [Lactose Dehydrogenase] activities in cultures in which the carbon sources were controlled." (Page 100, lines 4-6).

Fleury is summarized above.

Johnson discloses a "stochastic reinforcement, learning-based control system [ ] developed and applied to the supervision of uncharacterized, moderately thermophilic bacterial culture in a continuous stirred tank reactor (CSTR). The inventive system had as a process goal, e.g. to optimize the production of oxidized iron." (Col. 3, lines 38-42). "The control system has the ability to select environmental set point conditions, maintain those set points, analyze system states, and to recognize and diagnose instrument faults for the operator." (Col. 3, lines 44-47).

In making the rejection, the Examiner asserted that "[c]laim 1, step (c), now recites 'adjusting the amount ... with an optimization routine, wherein a ratio ... is treated as a separate control variable but is adjusted simultaneously.' It is noted that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, *therefore the Examiner has interpreted this limitation broadly.*" (Paper No. 20061022 at 8) (emphasis added).

The Examiner asserted that Kurokawa discloses "a method for simultaneously controlling glucose and glutamine concentrations comprising the following:"

- An adaptive control algorithm (i.e. optimization routine) for adjusting the feed rates from real-time data at

every sampling time [p.98, col. 2, lines 29-32], as in amended claim 1 (a) and the elected species.

- Independent model parameters comprising ratios of feed concentrations [EQNs (9)-(12)], as in amended claim 1(c).

- Generation of time-variant flow charts and response times based on three control algorithms comprising control variables [Fig. 2 and 3], as in amended claim 4(a).

- Input variables comprising distinct response times represented as quotients [p.97, Equation (7)], as in amended claim 4(c).

(Paper No. 20061022 at 8).

The Examiner acknowledged, however, that Kurokawa "do[es] not specifically teach the use of a 'microorganism', ..." (*Id.* at 9).

To fill the acknowledged gap, the Examiner relied on Fleury for "teach[ing] a multi-feed system and modeling and control strategies for the transformation of D-sorbitol to L-Sorbose using the microorganism *Gluconobacter oxydans* (i.e. *suboxydans)* [p.313, col. 1, paragraph 1], ..." (*Id.*).

The Examiner further relied on Johnson "to support a reasonable expectation for one of ordinary skill in the art successfully combining the optimization method of Kurokawa et al. with the use of the microorganism *Gluconobacter oxydans,* as taught by Fluery et al., as Johnson et al. teaches both optimization routines for nutrient mixtures [29] and [31], as well as the use of minerals-processing microorganisms [9]." (*Id.*).

The Examiner then contended that "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to combine the optimization method of Kurokawa et al. with the use of *Gluconobacter oxydans* (i.e.

suboxydans) as taught by Fluery et al. resulting in the practice of the instant claimed invention with a reasonable expectation of success." (*Id.*).

With a view towards furthering prosecution, we note again that the subject matter of previously cancelled claim 6 has been ***explicitly*** incorporated into claim 1, from which claims 3, 4, 7, and 8 either directly or indirectly depend.

In particular, claim 1 now recites "[a] method of optimizing performance of a fermentation process involving a complex nutrient mixture comprising:

(a) calculating a feed concentration of the complex nutrients;

(b) periodically stopping a supply of each nutrient in a complex nutrient mixture to a culture of microorganisms until a metabolic activity of the microorganisms decreases by a preset percentage;

and

(c) adjusting the amount of each nutrient supplied to the microorganism with an optimization routine, *wherein a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients is calculated and the feed concentration of the complex nutrients and the total quantity of the complex nutrients are treated as separate control variables that are calculated and adjusted simultaneously*." With these amendments, the Examiner's concern regarding claim 1, *i.e.*, "that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients," is rendered moot.

It is well settled that the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ

785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO must include evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the documents relied on by the Examiner as evidence of obviousness. *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). The factual inquiry whether to combine documents must be thorough and searching. And, as is well settled, the teaching, motivation, or suggestion to combine "***must be based on objective evidence of record***." *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002).

The rejection is devoid of *any* evidence - or even argument - in support of the proposed combination. All that is there is a conclusory statement that "it would have been obvious to someone of ordinary skill." What the rejection should have done, but did not, was to explain on the record ***why*** one skilled in this art would modify the disclosure of Kurokawa using Fluery and Johnson to arrive at the claimed method. As is well settled, an Examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done. *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993). Thus, the rejection is legally deficient and should be withdrawn for this reason alone.

Notwithstanding the legally insufficient nature of the rejection, we note that the rejection is also factually insufficient to support a rejection under § 103(a). In doing

so we observe that obviousness cannot be based upon speculation, nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (CCPA 1970). When a conclusion of obviousness is not based upon facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (BPAI 1993). Further, "to establish *prima facie* obviousness of a claimed invention, ***all claim limitations must be taught or suggested by the prior art***." MPEP § 2143.03 (citing *In re Royka*, 180 USPQ 580 (CCPA 1974)) (emphasis added).

Assuming *arguendo* that Kurokawa is properly combinable with Fleury and Johnson, which it is not, such a combination does not produce amended claim 1, from which claims 3, 4, 7, and 8 either directly or indirectly depend. As noted above, Kurokawa discloses "[a]n online system using HPLC [ ] developed for the measurement of glucose, glutamine, and lactate in a culture broth." (Abstract). Figure 3 of Kurokawa shows the results of the "[g]lucose concentration [ ] controlled at 0.2 g/l ... using [an] adaptive control strategy." (Page 98, lines 37-38). "Table II shows a comparison of LDH [Lactose Dehydrogenase] activities in cultures in which the carbon sources were controlled." (Page 100, lines 4-6). The rejection does not - and cannot - identify where in Kurokawa "*a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***is calculated*** *and the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***are treated as separate control variables that are calculated and adjusted simultaneously***" as recited in amended claim 1.

It is respectfully submitted that Kurokawa does not disclose or suggest currently amended claim 1. Unfortunately for the Examiner, neither Johnson nor Fleury fill this factual gap. As discussed above, Johnson discloses a "control system [that] has the ability to select environmental set point conditions, maintain those set points, analyze system states, and to recognize and diagnose instrument faults for the operator" in order "to optimize the production of oxidized iron," which is not even close to the method of optimizing performance of a fermentation process involving a complex nutrient mixture as recited in amended claim 1. (Col. 3, lines 35-47). Fleury, on the other hand, as implicitly acknowledged by the Examiner (*i.e.*, claim 6 was not rejected under §102 [Paper 02062006 at 5-6]), fails to disclose, *inter alia*, "*a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***is calculated*** *and the feed concentration of the complex nutrients and the total quantity of the complex nutrients* ***are treated as separate control variables that are calculated and adjusted simultaneously***." Rather, Fleury focuses on the bioxidation of D-sorbitol to L-sorbose. Thus, the proposed combination falls short of filling the factual gap in Kurokawa. For this reason also, the rejection should be withdrawn.

In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

For the foregoing reasons, favorable action on the merits, including entry of the amendments, withdrawal of the rejections, and allowance of all the claims, respectfully is requested. If the Examiner has any questions regarding this paper, please contact the undersigned attorney.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box. 1450 Alexandria, VA 22313-1450, on April 18, 2007.

Charles M. Avigliano, Reg. No. 52,578

Respectfully submitted,

By: Charles M. Avigliano

Charles M. Avigliano
Registration No. 52,578
BRYAN CAVE LLP
1290 Avenue of the Americas
New York, NY 10104-3300
Tel: (212) 541-2000
Fax: (212) 541-4630